

Amendments to the Claims

1.-9. (Canceled)

10. (currently amended) A method for treating female sexual arousal disorder comprising:

orally administering to a female subject in need thereof, an effective amount of an estrogen agonist / antagonist, and further comprising orally co-administering a cyclic guanosine 3',5'-monophosphate elevator.

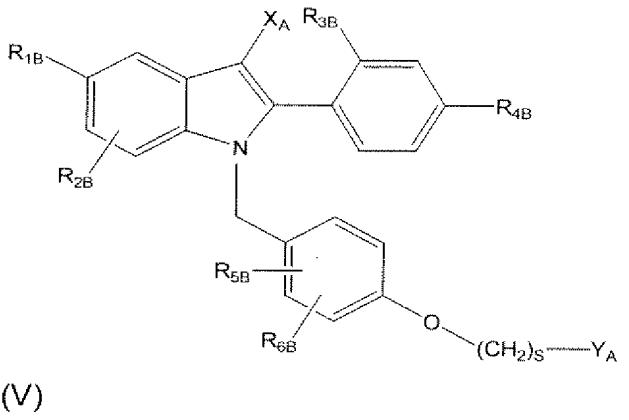
11. (previously presented) The method of claim 10 wherein said cyclic guanosine 3',5'-monophosphate elevator is a PDE<sub>V</sub> phosphodiesterase inhibitor.

12. (previously presented) The method of claim 11 wherein the PDE<sub>V</sub> phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

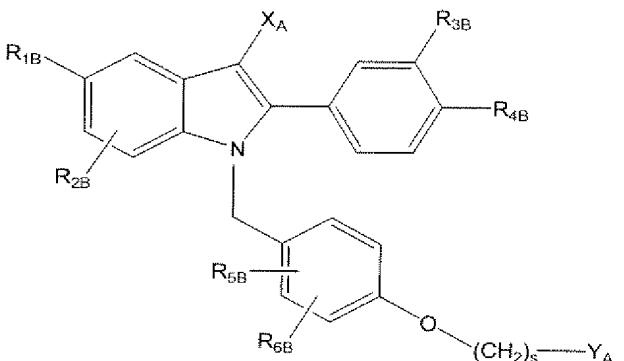
Claims 13.-39. (canceled)

40. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604, or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or prodrug thereof.

41. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:



(V)



(VI)

wherein:

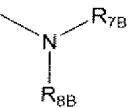
$R_{1B}$  is selected from H, OH, -O-C(O)-C<sub>1</sub>-C<sub>12</sub> alkyl (straight chain or branched), -O-C<sub>1</sub>-C<sub>12</sub> alkyl (straight chain or branched or cyclic), or halogens or C<sub>1</sub>-C<sub>4</sub> halogenated ethers,

$R_{2B}$ ,  $R_{3B}$ ,  $R_{4B}$ ,  $R_{5B}$ , and  $R_{6B}$  are independently selected from H, OH, -O-C(O)-C<sub>1</sub>-C<sub>12</sub> (straight chain or branched), -O-C<sub>1</sub>-C<sub>12</sub> (straight chain or branched or cyclic), halogens, or C<sub>1</sub>-C<sub>4</sub> halogenated ethers, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when  $R_{1B}$  is H,  $R_{2B}$  is not OH;

$X_A$  is selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, cyano, nitro, trifluoromethyl, and halogen;

s is 2 or 3;

$Y_A$  is the moiety:

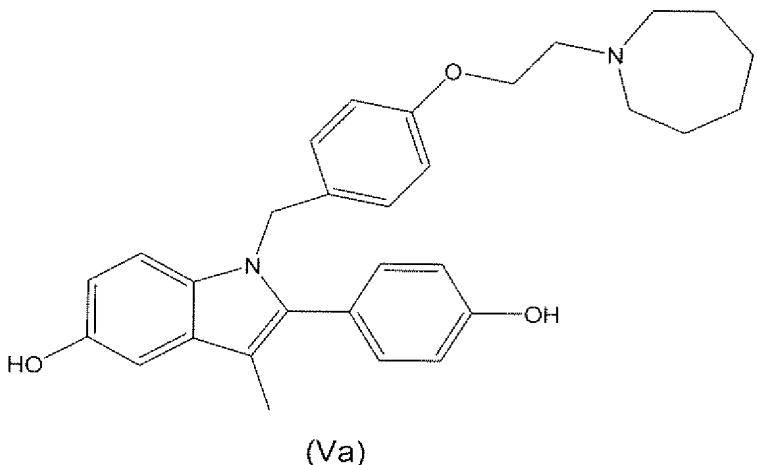


wherein:

- a) R<sub>7B</sub> and R<sub>8B</sub> are independently selected from the group of H, C<sub>1</sub>-C<sub>6</sub> alkyl, or phenyl optionally substituted by CN, C<sub>1</sub>-C<sub>6</sub> alkyl (straight chain or branched), C<sub>1</sub>-C<sub>6</sub> alkoxy (straight chain or branched), halogen, -OH, -CF<sub>3</sub>, or -OCF<sub>3</sub>; or
- b) R<sub>7B</sub> and R<sub>8B</sub> are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, trihalomethyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, trihalomethoxy, C<sub>1</sub>-C<sub>4</sub> acyloxy, C<sub>1</sub>-C<sub>4</sub> alkylthio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl, hydroxy (C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO<sub>2</sub>H, -CN, -CONHR<sub>1B</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NHSO<sub>2</sub>R<sub>1B</sub>, -NHCOR<sub>1B</sub>, -NO<sub>2</sub>, or phenyl optionally substituted with 1-3 (C<sub>1</sub>-C<sub>4</sub>)alkyl; or
- c) R<sub>7B</sub> and R<sub>8B</sub> are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, trihalomethyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, trihalomethoxy, C<sub>1</sub>-C<sub>4</sub> acyloxy, C<sub>1</sub>-C<sub>4</sub> alkylthio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl, hydroxy (C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO<sub>2</sub>H, -CN, -CONHR<sub>1B</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NHSO<sub>2</sub>R<sub>1B</sub>, -NHCOR<sub>1B</sub>, -NO<sub>2</sub>, or phenyl optionally substituted with 1-3 (C<sub>1</sub>-C<sub>4</sub>)alkyl; or
- d) R<sub>7B</sub> and R<sub>8B</sub> are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, trihalomethyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, trihalomethoxy, C<sub>1</sub>-C<sub>4</sub> acyloxy, C<sub>1</sub>-C<sub>4</sub> alkylthio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl, hydroxy (C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO<sub>2</sub>H, -CN, -CONHR<sub>1B</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NHSO<sub>2</sub>R<sub>1B</sub>, -NHCOR<sub>1B</sub>, -NO<sub>2</sub>, or phenyl optionally substituted with 1-3 (C<sub>1</sub>-C<sub>4</sub>)alkyl; or

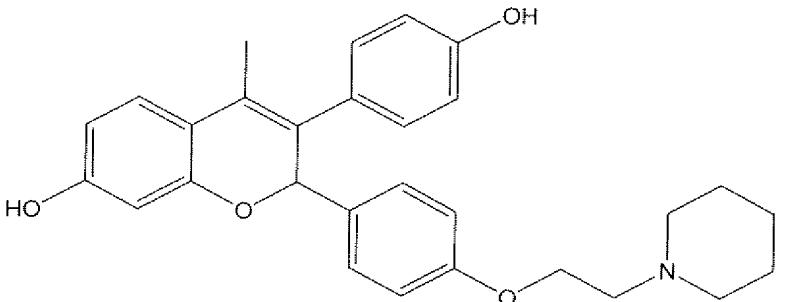
- e) R<sub>7B</sub> and R<sub>8B</sub> are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, trihalomethyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, trihalomethoxy, C<sub>1</sub>-C<sub>4</sub> acyloxy, C<sub>1</sub>-C<sub>4</sub> alkylthio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl, hydroxy (C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO<sub>2</sub>H, -CN, -CONHR<sub>1</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NHSO<sub>2</sub>R<sub>1B</sub>, -NHCOR<sub>1B</sub>, -NO<sub>2</sub>, or phenyl optionally substituted with 1-3 (C<sub>1</sub>-C<sub>4</sub>)alkyl; or
- f) R<sub>7B</sub> and R<sub>8B</sub> are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, trihalomethyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, trihalomethoxy, C<sub>1</sub>-C<sub>4</sub> acyloxy, C<sub>1</sub>-C<sub>4</sub> alkylthio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl, C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl, hydroxy (C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO<sub>2</sub>H, -CN, -CONHR<sub>1B</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)<sub>2</sub>, -NHSO<sub>2</sub>R<sub>1B</sub>, -NHCOR<sub>1B</sub>, -NO<sub>2</sub>, or phenyl optionally substituted with 1-3 (C<sub>1</sub>-C<sub>4</sub>)alkyl; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

42. (previously presented) The method of claim 41 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:

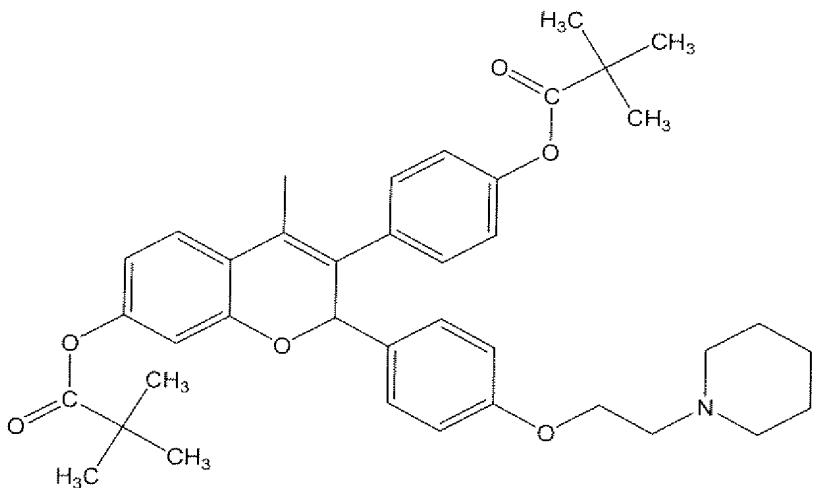


or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

43. (previously presented) The method of claim 10 wherein said estrogen agonist / antagonist is EM-652 of formula III below or is EM-800 of formula IV below:



(III)



(IV)

or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

44. – 45. (Canceled)

46. (currently amended) A method for treating female sexual arousal disorder comprising:

orally administering to a female subject in need thereof, an effective amount of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof and further comprising orally co-administering an effective amount of a cyclic guanosine 3',5'-monophosphate elevator.

47. (previously presented) The method of claim 46 wherein the cyclic guanosine 3',5'-monophosphate elevator is a PDE<sub>v</sub> phosphodiesterase inhibitor.

48. (previously presented) The method of claim 47 wherein the PDE<sub>v</sub> phosphodiesterase inhibitor is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

49. (canceled)

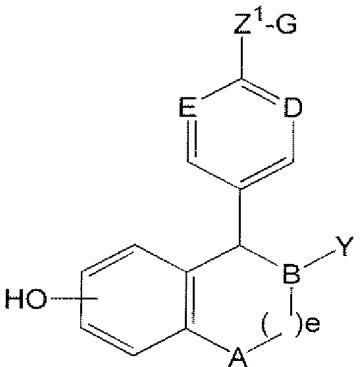
50. (previously presented) The method of claim 46, 47 or 48 wherein (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol, D-tartrate salt is administered.

51. (previously presented) The method of claim 48 wherein the female subject is pre-menopausal.

52. (previously presented) The method of claim 46 wherein the female subject is postmenopausal.

53. (previously presented) The method of claim 46 wherein the female subject is pre-menopausal.

54. (previously presented) The method of claim 10 wherein the estrogen agonist/antagonist is a compound of formula (I):



(I)

wherein:

A is selected from  $\text{CH}_2$  and NR;

B, D and E are independently selected from CH and N;

Y is

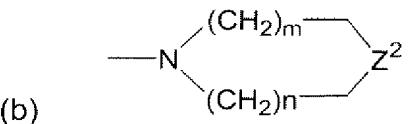
- (a) phenyl, optionally substituted with 1-3 substituents independently selected from  $R^4$ ;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from  $R^4$ ;
- (c)  $C_3\text{-}C_8$  cycloalkyl, optionally substituted with 1-2 substituents independently selected from  $R^4$ ;
- (d)  $C_3\text{-}C_8$  cycloalkenyl, optionally substituted with 1-2 substituents independently selected from  $R^4$ ;
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of  $-\text{O}-$ ,  $-\text{NR}^2-$  and  $-\text{S}(\text{O})_n-$ , optionally substituted with 1-3 substituents independently selected from  $R^4$ ;
- (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of  $-\text{O}-$ ,  $-\text{NR}^2-$  and  $-\text{S}(\text{O})_n-$  optionally substituted with 1-3 substituents independently selected from  $R^4$ ; or
- (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of  $-\text{O}-$ ,  $-\text{NR}^2-$  and  $-\text{S}(\text{O})_n-$ , optionally substituted with 1-3 substituents independently selected from  $R^4$ ;

$Z^1$  is

- (a)  $-(CH_2)_p W(CH_2)_q-$ ;
- (b)  $-O(CH_2)_p CR^5R^6-$ ;
- (c)  $-O(CH_2)_p W(CH_2)_q-$ ;
- (d)  $-OCHR^2CHR^3-$ ; or
- (e)  $-SCHR^2CHR^3-$ ;

G is

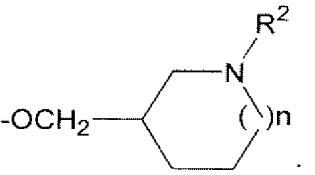
- (a)  $-NR^7R^8-$ ;



wherein n is 0, 1 or 2; m is 1, 2 or 3; Z<sup>2</sup> is -NH-, -O-, -S-, or -CH<sub>2</sub>-;

optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R<sup>4</sup>; or

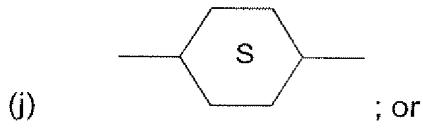
(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>; or



Z<sup>1</sup> and G in combination may be

W is

- (a)  $-CH_2-$ ;
- (b)  $-CH=CH-$ ;
- (c)  $-O-$ ;
- (d)  $-NR^2-$ ;
- (e)  $-S(O)_n-$ ;
- (f)  $\begin{array}{c} O \\ || \\ C \end{array}$ ;
- (g)  $-CR^2(OH)-$ ;
- (h)  $-CONR^2-$ ;
- (i)  $-NR^2CO-$ ;



(k) -C≡C-;

R is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>2</sup> and R<sup>3</sup> are independently

- (a) hydrogen; or
- (b) C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>4</sup> is

- (a) hydrogen;
- (b) halogen;
- (c) C<sub>1</sub>-C<sub>6</sub> alkyl;
- (d) C<sub>1</sub>-C<sub>4</sub> alkoxy;
- (e) C<sub>1</sub>-C<sub>4</sub> acyloxy;
- (f) C<sub>1</sub>-C<sub>4</sub> alkylthio;
- (g) C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl;
- (h) C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl;
- (i) hydroxy (C<sub>1</sub>-C<sub>4</sub>)alkyl;
- (j) aryl (C<sub>1</sub>-C<sub>4</sub>)alkyl;
- (k) -CO<sub>2</sub>H;
- (l) -CN;
- (m) -CONHOR;
- (n) -SO<sub>2</sub>NHR;
- (o) -NH<sub>2</sub>;
- (p) C<sub>1</sub>-C<sub>4</sub> alkylamino;
- (q) C<sub>1</sub>-C<sub>4</sub> dialkylamino;
- (r) -NHSO<sub>2</sub>R;
- (s) -NO<sub>2</sub>;
- (t) -aryl; or
- (u) -OH;

R<sup>5</sup> and R<sup>6</sup> are independently C<sub>1</sub>-C<sub>8</sub> alkyl or together form a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring;

R<sup>7</sup> and R<sup>8</sup> are independently

- (a) phenyl;
- (b) a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring, saturated or unsaturated;
- (c) a C<sub>3</sub>-C<sub>10</sub> heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
- (d) H;
- (e) C<sub>1</sub>-C<sub>6</sub> alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with R<sup>5</sup> or R<sup>6</sup>;

R<sup>7</sup> and R<sup>8</sup> in either linear or ring form may optionally be substituted with up to three substituents independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by R<sup>7</sup> and R<sup>8</sup> may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

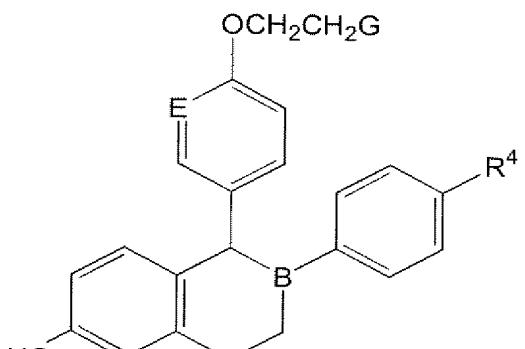
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

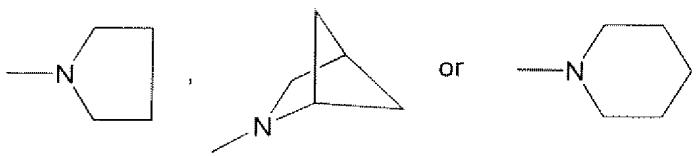
q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

55. (previously presented) The method of claim 54 wherein said estrogen agonist / antagonist is a compound of formula (IA):



(IA)



wherein G is

$R^4$  is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.